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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,392	12/19/2005	Fernando Bouffard Fita	14455.876US01	8090

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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,392	FITA, FERNANDO BOUFFARD	
	Examiner	Art Unit	
	JODY L. KAROL	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-12,14,15,17,19,20,22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-12,14,15,17,19,20,22 and 24-26* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/EP04/50967 International Filing Date: 6/1/2004 which claims priority to Spain P200301548. In a preliminary amendment dated 12/19/2005, claims 6, 13, 16, 18, 21, and 23 have been cancelled and claims 2-5, 7-12, 14-15, 17, 19-20, 22, and 26 have been amended. Accordingly, claims 1-5, 7-12, 14-15, 17, 19-20, 22, and 24-26 are pending and examined on the merits herein.

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on Application No. P200301548 filed in Spain on 6/13/2003.

Information Disclosure Statement

2. The information disclosure statement (IDS) filed on 12/19/2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered.

Specification

3. The abstract of the disclosure is objected to because the recitation of “it” as the first word in the first sentence is unclear. The Examiner suggests changing "It comprises" to “Compositions comprising” to obviate this objection. Correction is required. See MPEP § 608.01(b).

4. The use of the trademark Tween® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claim 17 is objected to because of the following informalities: “hydrolurodinase” is apparently misspelled. The proper spelling should be "hydoluronidase." Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 and 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 contains the trademark/trade name Tween®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of

35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe polysorbates and, accordingly, the identification/description is indefinite.

Claim 26 is unclear in that it claims a method of use of a composition comprising lidocaine, prilocaine, and tetracaine for the preparation of a topical composition, but contains steps directed to both the preparation of said composition and a method of administering said composition. Therefore, it is unclear if Applicant intends to claim a method for preparing said composition, or a method of using said composition. Accordingly, the metes and bounds of the claim cannot be ascertained by one of ordinary skill in the art.

For examination purposes, and in the interest of compact prosecution, the claim will be interpreted as method of using said composition (i.e. for the eliciting an anesthetic effect) comprising applying the composition topically.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-5, 7-12, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cassel (US 2002/0128285).

The instant claims are directed to compositions for topical administration comprising therapeutically safe and effective amounts of lidocaine, prilocaine, and tetracaine or pharmaceutically acceptable salts thereof.

Cassel teaches topical delivery of a local anesthetic in a pharmaceutically acceptable topical drug formulation to an exterior surface of a surgically closed wound (see abstract and page 2, section [0025]). Cassel further teaches that the preferred local anesthetics include lidocaine, prilocaine, and tetracaine (see page 2, section [0028]) and that the local anesthetics may be combined in a pharmaceutically acceptable topical formulation, with a preferred combination containing lidocaine and prilocaine, and another containing lidocaine and tetracaine (see page 3, section [0030]). Cassel also teaches lidocaine and

prilocaine as a eutectic mixture as claimed in the instant claim 3, wherein lidocaine is present in 1 to 40% by weight and prilocaine is present in 0.5 to 40% by weight, which overlaps or encompasses the ranges as claimed for these components in the instant claims 4-5, and 25 (see page 4, section [0057]). Cassel also teaches that the preferred amounts for the lidocaine and tetracine composition are lidocaine in 1 to 40% by weight and tetracaine in 0.5 to 40% by weight, which overlaps or encompasses the ranges as claimed for these components in the instant claims 4-5, 7, and 25 (see page 4, section [0058]). Cassel teaches that these compositions comprise carriers systems including buffered solutions (meaning the formulation contains water) or other art-known carriers, and that the any pharmaceutically acceptable excipient is acceptable, wherein the compositions are in the form of a gel, cream, or ointment as claimed in the instant claims 2, 8, and 24 (see page 3, section [0038] and page 4, section [0055], and page 5, section [0061]). Cassel teaches that penetration enhancers may be used in the formulations, and include N-methyl pyrrolidone as claimed in the instant claims 9-12, and 25 (see page 5, section [0065]). Cassel further teaches methods of using the compositions comprising topically applying the compositions to the exterior surface of a wounds as claimed in the instant claim 26 **as best understood** (see page 5, Example I, and claim 1 for example).

Cassel does not explicitly teach a composition comprising a combination of lidocaine, prilocaine, and tetracaine. Cassel also does not explicitly teach compositions comprising the amounts of the components (i.e. anesthetics and methyl pyrrolidone) as claimed in the instant claims 4-5, 7, 11-12, and 25.

However, it would have been obvious to one of ordinary skill in the art at the time of the invention, to combine the lidocaine/prilocaine composition with the lidocaine/tetracaine composition as taught by Cassel, to form a third composition comprising all three anesthetic agents. One of ordinary skill in the art would have been motivated to do so because both prior art compositions have utility as topical anesthetic compositions, and the combination of the compositions is claimed to have utility as a topical anesthetic composition. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose (See *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980)).

Furthermore, while the references do not explicitly teach the claimed amounts of anesthetic agents or methyl pyrrolidone, the determination of optimal or workable amount of these components by routine experimentation is obvious absent showing of criticality of the claimed amounts. One having ordinary skill in the art would have been motivated to optimize the amounts of the herein claimed anesthetics in order to obtain a composition with the desired anesthetic properties and desired skin penetrating effect. Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

9. Claims 1-5, 7-9, 19-20, 22, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samuels et al. (US 2002/0006435 A1).

Samuels et al. teaches compositions for topical application comprising a therapeutically effective amount of topical anesthetic and a pharmaceutically carrier, and methods of administering the composition to a mammal (see abstract). Samuels et al. teaches that the compositions comprise 0.5 to 20% by weight of anesthetic agents, (see page 1, section [0015]), that preferred agents include lidocaine, prilocaine, and tetracaine, and that preferably the anesthetic is eutectic mixture of anesthetics (see page 2-3, section [0035]). In a specific embodiments, Samuels et al. teaches a eutectic mixture of 3.5 % by weight lidocaine, 2.5% by weight prilocaine, and 1.5% by weight dibucaine (see page 3, section [0039], and page 8, Example 4), a eutectic mixture of 2.5% by weight lidocaine and 2.5% by weight prilocaine also comprising water as claimed in the instant claims 2-3 (see page 3, sections [0040]-[0041] and page 8, Example 5), and a mixture 12% by weight lidocaine and 12% by weight tetracaine hydrochloride (see page 9, Example 6). Samuels et al. further teaches that the compositions may be formulated as creams, lotions solutions, gels or sprays, and contains carriers such as emollients, emulsifiers, thickening agents, surfactants, etc. as claimed in the instant claims 8-9, and 24 (see page 4, section [0056]). Samuels et al. teaches that thickeners include gelling agents such as carbopol (carbomer), and that gums such as guar gum may also be incorporated into the composition as claimed in the instant claims 19-20 and 25 (see page 4, section [0060] and page 7, section [0100]. Samuels et al. further teaches that the compositions may comprise 0.5 to 2% by weight surfactant, and include nonionic surfactant such as polysorbate 20 (Tween 20), and polysorbate 80 (Tween 80)

as claimed in the instant claims 9, 2, and 25 (see page 5, sections [0070] and [0073]). Samuels et al. also teaches methods of administering the composition comprising contacting the skin with said composition as claimed in the instant claim 26 **as best understood** (see page 7, sections [0108]-[0110]).

Samuels et al. does not explicitly teach a composition comprising a combination of lidocaine, prilocaine, and tetracaine. Samuels et al. also does not explicitly teach compositions comprising the amounts of the components (i.e. anesthetics and methyl pyrrolidone) as claimed in the instant claims 4-5, 7, 19-20 and 25.

However, it would have been obvious to one of ordinary skill in the art at the time of the invention, to combine the lidocaine/prilocaine composition with the lidocain/ tetracaine composition as taught by Samuels et al., to form a third composition comprising all three anesthetic agents. One of ordinary skill in the art would have been motivated to do so because both prior art compositions have utility as topical anesthetic compositions, and the combination of the compositions is claimed to have utility as a topical anesthetic composition. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose (See *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980)).

Furthermore, while the references do not explicitly teach the claimed amounts of anesthetic agents or viscosity increasing agent (thickener), the determination of optimal or workable amount of these components by routine experimentation is obvious absent showing of criticality of the claimed amounts.

One having ordinary skill in the art would have been motivated to do this in order to obtain a composition with the desired anesthetic properties and viscosity. Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

10. Claims 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cassel (US 2002/0128285) as applied to claims 1-5, 7-12, 24, and 26 above, and further in view of Lutz et al. (US 5,750,139).

Cassel is described above as applied to claims 1-5, 7-12, 24, and 26.

Cassel does not teach teach dimethyl sulfoxide, nor its amount present in the composition, as a penetration enhancer as claimed in the instant claims 14-15. Lutz et al. teaches that suitable solvents having penetration-enhancing properties are skin-tolerated penetration enhancers such as dimethyl sulfoxide (DMSO) or N-methylpyrrolidone (see column 8, lines 44-49).

It would have been obvious to one of ordinary skill in the art at the time of the invention, to substitute DMSO for N-methypyrrolidone in the compositions taught and made obvious by Cassel. One of ordinary skill in the art would have been motivated to do because both DMSO and methyl pyrrolidone are art-recognized penetration enhancers as taught by Lutz et al. Furthermore, the determination of optimal or workable amount of DMSO by routine experimentation is obvious absent showing of criticality of the claimed amount. One having ordinary skill in the art would have been motivated to optimize the amount of DMSO in order to obtain a composition with the desired skin-

penetrating effects. Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

11. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cassel (US 2002/0128285) as applied to claims 1-5, 7-12, 24, and 26 above, and further in view of Santana et al. (US 2003/0103955 A1).

Cassel is described above as applied to claims 1-5, 7-12, 24, and 26.

Cassel does not teach hyaluronidases or derivatives of mucopolysaccharides as a spreading agent in the compositions as claimed in the instant claim 17.

Santana et al. teaches topical compositions comprising diclofenac, papain, hyalurodinase, and vitamin E (see abstract). Santana et al. further teaches that the use of hyalurodinase as a diffusion factor (spreading agent) is known, and is compositions comprising the hyalurodinase have a high rate of penentration through the skin (see page 1, section [0012] and page 2, section [0016]).

It has been held that the selection of a known material based on its suitability for its intended use supported a *prima facia* obviousness determination in *Sinclair & Carroll Co. V. Interchemical Corp.,* 325 U.S. 327, 65 USPQ 297 (1945). Accordingly it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the compositions taught or made obvious by Cassel by adding the spreading agent hyaluronidase as taught by Santana et al.

One of ordinary skill in the art would have a reasonable expectation of success in combining the above recited components, since it has been reasoned that reading a list and selecting a known compound to meet known requirements in no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle. *Sinclair & Carroll Co.,* 325 U.S. at 335, 65 USPQ at 301. Since all elements of the instant claims are taught in the cited references to be employed in topical compositions, combining the components for their intended use would have been *prima facia* obvious.

12. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cassel (US 2002/0128285) and Samuels et al. (US 2002/0006435 A1) in view of Lutz et al. (US 5,750,139) and Santana et al. (US 2003/0103955 A1).

Cassel is described above as applied to claims 1-5, 7-12, 24, and 26.

Samuels et al. is described above as applied to claims 1-5, 7-9, 19-20, 22, 24, and 26.

Neither Cassel nor Samuels et al. explicitly teach a composition containing all the specific components and their weight percentages as claimed in the instant claim 25. Cassel and Samuels et al. also do not teach compositions comprising DMSO and hyaluronidase.

As described above, Lutz et al. teaches DMSO as a penetration enhancer in topical compositions and Santana et al. teaches the use of hyaluronidase in topical compositions.

The teachings of Cassel, Sameuls et al, Lutz et al. and Santana et al. are considered to be in the same field of endeavor because they all provide for compositions used for topical administration.

As reasoned above, it has been held that the selection of a known material based on its suitability for its intended use supported a *prima facia* obviousness determination in *Sinclair & Carroll Co. V. Interchemical Corp.,* 325 U.S. 327, 65 USPQ 297 (1945). Accordingly it would have been obvious to one of ordinary skill in the art at the time of the invention to modify and/or combine the compositions taught or made obvious by Cassel and Sameuls et al. by adding the penetration DMSO as taught by Lutz et al. and the spreading agent hyaluronidase as taught by Santana et al.

One of ordinary skill in the art would have a reasonable expectation of success in combining the above recited components, since it has been reasoned that reading a list and selecting a known compound to meet known requirements in no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle. *Sinclair & Carroll Co.,* 325 U.S. at 335, 65 USPQ at 301. Since all elements of the instant claims are taught in the cited references to be employed in topical compositions, combining the components for their intended use would have been *prima facia* obvious, absent evidence to the contrary.

Lastly, the optimization of the components present in the composition is addressed in *In re Aller*, 220 F.2d 454, 105 U.S.P.Q. 233 (C.C.P.A. 1955). Accordingly, absence of a showing of unexpected results, discovery of an optimum variable in a known invention is obvious when the parameter optimized

is recognized as a result-effective variable. Therefore, the optimization of the various well-known components of the instant invention is well within the level of ordinary skill in the art, and a matter of routine experimentation.

Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JODY L. KAROL whose telephone number is (571)270-3283. The examiner can normally be reached on 8:30 am - 5:00 pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

JLK

/San-ming Hui/
Primary Examiner, Art Unit 1617